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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/730,771	12/08/2003	Jian-Bing Fan	WIBL-P02-516	3260

7590 08/10/2006

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EXAMINER	
WHISENANT, ETHAN C	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/730,771	FAN ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant, Ph.D.	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 December 2003 and 10 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

NON-FINAL ACTION

1. The applicant's Preliminary Amendment filed 10 MAY 04 has been entered. Following the entry of the Preliminary Amendment, **Claim(s) 1-10 and 12-41** is/are pending.

SEQUENCE RULES

2. This application complies with the sequence rules and the sequences have been entered by the Scientific and Technical Information Center.

35 USC § 112- 2nd Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH

4. **Claim(s) 1, 33-41** rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the phrase "the other three types of ddNTPs" lacks proper antecedent basis.

Claim 1 is indefinite in view of the use of the word "complementarysequence" on line 23. This appears to be a simple typographical error,

therefore, it should be noted that the examiner has interpreted this word as the phrase "complementary sequence" for the evaluation of this claim against the prior art.

Claims 33-41 are confusing in light of the phrase " of any one of ."

35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 103

7. Claim(s) 1-6, 12-19, 21-22, 31-32 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugozzoli et al.(1992) in view of Lapidus et al. [US 5,928,870 (1999)].

Ugozzoli et al. teach a method of genotyping comprising all of the limitations recited in Claim 1 except Ugozzoli et al. do not teach subjecting the target nucleic acid / locus-specific tagged oligonucleotide complex to a single base extension reaction in the presence of two or more labelled ddNTPs wherein each type of labeled ddNTP carries a label that can be distinguished from the label on any other type of ddNTP. See at least for example Figure 1 of Ugozzoli et al. However, Lapidus et al. do teach a method wherein a target nucleic acid / locus-specific oligonucleotide complex is subjected to a single base extension reaction in the presence of two or more labelled ddNTPs wherein each type of labeled ddNTP carries a label that can be distinguished from the label on any other type of ddNTP. See the paragraph bridging Columns 5-6. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ugozzoli et al. wherein the target nucleic acid / locus-specific tagged oligonucleotide complex to a single base extension reaction in the presence of two or more labelled ddNTPs wherein each type of labeled ddNTP carries a label that can be distinguished from the label on any other type of ddNTP. The ordinary artisan would have been motivated to modify Ugozzoli et al. with Lapidus et al. in order to eliminate the need for the two-four separate primer extension reactions required by Ugozzoli et al.

Claim 2 is drawn to a method to aid in determining a ratio of alleles at a polymorphic locus which method is essentially the same as that recited in Claim 1 except that the method of Claim 2 requires the use of a pair of primers to amplify a region of a nucleic acid in a sample, wherein the region comprises a polymorphic locus.

In addition the method of Claim 2 further requires that the locus-specific tagged oligonucleotide comprise a 5' region not complementary to the amplified DNA product.

Ugozzoli et al. teach both of these limitations.

Claim 3 is drawn to an embodiment of Claim 2 wherein two complementary strands of the amplified DNA product are present in the single base extension reaction.

Ugozzoli et al. teach this limitation. See, at least, for example, the first column on p.109.

Claim 4 is drawn to an embodiment of Claim 2 wherein two complementary strands of the amplified DNA product are present in the step of labeling.

Ugozzoli et al. teach this limitation. See, at least, for example, the first column on p.109.

Claim 5 is drawn to an embodiment of Claim 2 wherein the label is a fluorescent label.

Lapidus et al. teach this limitation. See, at least, for example, the Column 14, beginning at about line 41.

Claim 6 is drawn to an embodiment of Claim 2 wherein the label is a radiolabel.

Lapidus et al. teach this limitation. See, at least, for example, the Column 14, beginning at about line 41.

Claim 12 is drawn to an embodiment of Claim 2 wherein the step of labeling employs four distinct dideoxynucleotides bearing distinct labels.

Ugozzoli et al. in view of Lapidus teach a method of genotyping comprising all of the step of Claim 12 except these authors never explicitly teach employing four distinct dideoxynucleotides bearing distinct labels. Lapidus et al. teach using at least two of the four common dideoxynucleotide. See, at least, for example, the paragraph bridging Columns 5-6.

Claim 13 is drawn to an embodiment of Claim 2 further comprising the step of comparing the quantities of a first and second label at a location on the solid support and determining the ratio of the nucleotides present at the polymorphic locus in the sample.

Ugozzoli et al. in view of Lapidus et al. make this embodiment *prima facie* obvious. See, at least, for example, the paragraph bridging Columns 5-6 of Lapidus et al. and Figure 1 of Ugozzoli et al.

Claim 14 is drawn to an embodiment of Claim 13 wherein the ratio of nucleotides at two or more polymorphic loci is determined simultaneously.

Ugozzoli et al. reasonably suggest this limitation wherein these authors teach "AS-PE capture offers the possibility of detecting multiple templates and multiple samples simultaneously." See the bottom of Column 2 on page 107.

Claim 15 is drawn to an embodiment of Claim 2 wherein the sample comprises DNA from two or more individuals.

Ugozzoli et al. reasonably suggest this limitation wherein these authors teach "AS-PE capture offers the possibility of detecting multiple templates and multiple samples simultaneously." See the bottom of Column 2 on page 107.

Claim 16 is drawn to an embodiment of Claim 15 wherein the ratio of nucleotides present at two or more polymorphic loci is determined simultaneously.

Ugozzoli et al. reasonably suggest this limitation wherein these authors teach "AS-PE capture offers the possibility of detecting multiple templates and multiple samples simultaneously." See the bottom of Column 2 on page 107.

Claim 17 is drawn to an embodiment of Claim 2 wherein the solid support is selected from a defined group which includes an oligonucleotide array.

Ugozzoli et al. reasonably suggest this limitation. See at least for example Figure 1.

Claim 18 is drawn to a method to aid in determining a ratio of alleles at a polymorphic locus which method comprises essentially the same steps as that recited in Claim 1 except that the method of Claim 18 requires that the locus-specific tagged oligonucleotide comprise a 5' region not complementary to the target DNA molecule containing the polymorphic locus.

As argued previously Ugozzoli et al. teach this limitation. See Figure 1 and note that the 5' end of the extension primer is not complementary to the target DNA molecule containing the polymorphic locus but rather to a nucleotide sequence on an oligonucleotide array.

Claim 19 is drawn to an embodiment of Claim 18 wherein two complementary strands of DNA molecule are present in the single base extension reaction.

Ugozzoli et al. teach this limitation. See, at least, for example, the first column on p.109.

Claim 21 is drawn to an embodiment of Claim 18 wherein the label is a fluorescent label.

Lapidus et al. teach this limitation. See, at least, for example, the Column 14, beginning at about line 41.

Claim 22 is drawn to an embodiment of Claim 18 wherein the label is a radiolabel.

Lapidus et al. teach this limitation. See, at least, for example, the Column 14, beginning at about line 41.

Claim 31 is drawn to an embodiment of Claim 18 wherein the step of labeling employs at least two distinct dideoxynucleotides bearing distinct labels.

Lapidus et al. teach this limitation. See, at least, for example, the paragraph bridging Columns 5-6.

Claim 32 is drawn to an embodiment of Claim 18 wherein the step of labeling employs at least four distinct dideoxynucleotides bearing distinct labels.

Ugozzoli et al. in view of Lapidus et al. make this embodiment *prima facie* obvious. See, at least, for example, the paragraph bridging Columns 5-6 and Column 14, beginning at about line 41 of Lapidus et al.

8. **Claim(s) 7-9, 23-25 and 33-41** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugozzoli et al.(1992) in view of Lapidus et al. [US 5,928,870 (1999)] as applied against Claim 2 and 18 above and further in view of Matthews et al. [Analytical Biochemistry 169: 1-25 (1988)].

Claim 7 is drawn to an embodiment of Claim 2 wherein the label is an enzyme label. **Claim 8** is drawn to an embodiment of Claim 2 wherein the label is an antigenic label. **Claim 9** is drawn to an embodiment of Claim 2 wherein the label is an affinity binding partner. **Claim 23** is drawn to an embodiment of Claim 18 wherein the label is an enzyme label. **Claim 24** is drawn to an embodiment of Claim 18 wherein the

label is an antigenic label. **Claim 25** is drawn to an embodiment of Claim 18 wherein the label is an affinity binding partner.

The combination of Ugozzoli et al. in view of Lapidus et al. reasonably suggest the method(s) comprising all of the limitations recited in Claims 7-9 and 23-25 except these authors do not teach or reasonably suggest an embodiment wherein the label is an enzyme label or an antigenic label or an affinity binding partner. However, as evidenced by at least Matthews et al. the use of enzyme labels, antigenic labels and affinity binding partner labels was well known prior to the instant invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method reasonably suggest by the combination of Ugozzoli et al. in view of Lapidus et al. wherein the radioactive labels of Ugozzoli et al. in view of Lapidus et al. are replaced by labels taught by Matthews et al. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Claim 33 is drawn to an embodiment of Claim 1 wherein the oligonucleotide array comprises at least 10 oligonucleotide tags fixed to a solid surface. **Claim 34** is drawn to an embodiment of Claim 1 wherein the oligonucleotide array comprises at least 100 oligonucleotide tags fixed to a solid surface **Claim 35** is drawn to an embodiment of Claim 1 wherein the oligonucleotide array comprises at least 1000 oligonucleotide tags fixed to a solid surface. **Claim 36** is drawn to an embodiment of Claim 2 wherein the oligonucleotide array comprises at least 10 oligonucleotide tags fixed to a solid surface. **Claim 37** is drawn to an embodiment of Claim 2 wherein the oligonucleotide array comprises at least 100 oligonucleotide tags fixed to a solid surface **Claim 38** is drawn to an embodiment of Claim 2 wherein the oligonucleotide array

comprises at least 1000 oligonucleotide tags fixed to a solid surface. **Claim 39** is drawn to an embodiment of Claim 18 wherein the oligonucleotide array comprises at least 10 oligonucleotide tags fixed to a solid surface. **Claim 40** is drawn to an embodiment of Claim 18 wherein the oligonucleotide array comprises at least 100 oligonucleotide tags fixed to a solid surface **Claim 41** is drawn to an embodiment of Claim 18 wherein the oligonucleotide array comprises at least 1000 oligonucleotide tags fixed to a solid surface.

The combination of Ugozzoli et al. in view of Lapidus et al. reasonably suggest the method(s) comprising all of the limitations recited in Claims 33-41 except these authors do not teach or reasonably suggest an embodiment wherein the solid support comprises at least 10, at least 100 or at least 1000 oligonucleotide tags. However, as evidenced by at least Brenner –see at least Claim 20 - the use of high density oligonucleotide arrays for sorting polynucleotides was well known prior to the instant invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method reasonably suggest by the combination of Ugozzoli et al. in view of Lapidus et al. wherein the oligonucleotide array comprises at least 10, at least 100 or at least 1000 oligonucleotide tags fixed to a solid surface. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

9. Claim(s) 10 and 26 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugozzoli et al.(1992) in view of Lapidus et al. [US 5,928,870 (1999)]

as applied against Claim 2 and 18 above and further in view of Pastinen et al. [Clinical Chemistry 42 (9) : 1391-1397 (1996)].

Claim 10 is drawn to an embodiment of Claim 2 further comprising the step of optically detecting a fluorescent label on the solid support. **Claim 26** is drawn to an embodiment of Claim 18 further comprising the step of optically detecting a fluorescent label on the solid support.

The combination of Ugozzoli et al. in view of Lapidus et al. reasonably suggest the method(s) comprising all of the limitations recited in Claims 10 and 26 except these authors do not teach or reasonably suggest an embodiment wherein a fluorescent label is optically detected However, as evidenced by at least Pastinen et al. the optical detection of a fluorescent label on the solid support was well known prior to the instant invention. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method reasonably suggest by the combination of Ugozzoli et al. in view of Lapidus et al. wherein the fluorescent labels of Ugozzoli et al. in view of Lapidus et al. are optically detected as taught by Pastinen et al. The ordinary artisan would have been motivated to modify the method reasonably suggested by combination of Ugozzoli et al. in view of Lapidus et al. in order to eliminate the need for radiolabels which can be hazardous.

10. Claim(s) 20 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugozzoli et al.(1992) in view of Lapidus et al. [US 5,928,870 (1999)] as applied against Claim 18-19 above and further in view of Bogdanov [US 6,245,507 (2001)].

Claim 20 is drawn to an embodiment of Claim 19 wherein each complementary strand is used as a template to label an extension primer.

The combination of Ugozzoli et al. in view of Lapidus et al. reasonably suggest the method comprising all of the limitations recited in Claims 20 except these authors do not teach or reasonably suggest an embodiment wherein each

complementary strand is used as a template to label an extension primer However, as evidenced by at least Bogdanov the genotyping of both strands of a target nucleic acid comprising a polymorphic site was well known prior to the instant invention. Note Column wherein Bogdanov teach "Preferably, analysis of both strands is performed to reduce potential mis-calling." Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method reasonably suggest by the combination of Ugozzoli et al. in view of Lapidus et al. wherein both strands of the target nucleic acid comprising the polymorphic site are used as template to label an extension primer. The ordinary artisan would have been motivated to modify the method reasonably suggested by combination of Ugozzoli et al. in view of Lapidus et al. with Bogdanov in order to reduce the potential for mis-calling the polymorphic site.

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CONCLUSION

11. **Claim(s) 1-10 and 12-41** is/are rejected and/or objected to for the reason(s) set forth above.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30AM - 5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

The Central Fax number for the USPTO is (571) 273-8300. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

ETHAN WHISENANT
PRIMARY EXAMINER
Art Unit 1634